NOTICE OF PROPOSED REGULATION ADOPTION
AND
INITIAL STATEMENT OF REASONS

California Code of Regulations
Title 17. – Public Health
Division 4 - California Institute For Regenerative Medicine
Chapter 2

Date: March 17, 2006

Deadline for Submission of Written Comment: May 1, 2006 – 5:00 p.m.

Hearing Date: May 1, 2006

Subject Matter of Proposed Regulations: Medical and Ethical Standards Applicable to CIRM-Funded Research and Training

Sections Affected:

The proposed regulations adopt Chapter 2 and sections 100010, 100020, 100030, 100040, 100050, 100060, 100070, 100080, 100090, 100100, 100110, 100120 and 100130 of Title 17 of the California Code of Regulations.

Authority: Article XXXV of the California Constitution and Health and Safety Code section 125290.40, subdivision (j).

Reference: Sections 439.900-439.906, 100237-100239, 24172, 125290.30, 125290.35, 125290.40, 124290.55, 125292.10, subds. (p)(q), 125300, 125315, Health and Safety Code.

Informative Digest/Policy Statement Overview:

The California Institute for Regenerative Medicine ("Institute" or "CIRM") was established in early 2005 with the passage of Proposition 71, the California Stem Cell Research and Cures Initiative. The statewide ballot measure, which provides $3 billion in funding for stem cell research and dedicated facilities at California universities and research institutions, was approved by California voters on November 2, 2004, called for the establishment of a new state agency to make grants and provide loans for stem cell research, research facilities and other vital research opportunities.

The Independent Citizens' Oversight Committee ("ICOC") is the 29-member governing board for the Institute. The ICOC members are public officials, appointed on the basis of their experience earned in California's leading public universities, non-profit academic and research institutions, patient advocacy groups and the biotechnology industry.

The Scientific and Medical Accountability Standards Working Group ("Standards Working Group") makes recommendations to the 29-member ICOC that governs the CIRM on scientific, medical and ethical standards pertaining to stem cell research the institute funds. Specifically, California Health and Safety Code section 125290.55 requires the Standards Working Group to: 1) recommend to the ICOC scientific, medical and ethical standards; 2) recommend to the ICOC standards for all medical, socioeconomic, and financial aspects of clinical trials and therapy delivery to patients, including, among others, standards for safe and ethical procedures for obtaining materials and cells for research and clinical efforts for the appropriate treatment of human subjects in medical research consistent with paragraph (2) of subdivision (b) of Section 125290.35, and to ensure compliance with patient privacy laws; 3) recommend to the ICOC modification of the standards described in numbers (1) and (2) as needed; 4) make recommendations to the ICOC on the oversight of funded research to ensure compliance with the standards described in numbers (1) and (2); 5) advise the ICOC, the Scientific and Medical Research Funding Working Group, and the Scientific and Medical Research Facilities Working Group on an on-going basis on relevant ethical and regulatory issues.

After five public meetings and three public sessions to solicit public comments from across the state, the Standards Working Group finalized these draft regulations on January 31, 2006 that were subsequently approved by the ICOC at its public meeting on February 10, 2006.

Under the proposed regulations, CIRM will be the first agency to: legally mandate specialized review by a Stem Cell Research Oversight (SCRO) committee; enhance state and federal policies in the areas of voluntary-informed consent; and ensure that women's reproductive needs are protected and prioritized before the research. These regulations reaffirm the requirements of Proposition 71, namely a ban on human reproductive cloning and a prohibition of payment to egg donors in the state of California.

The draft regulations adopt a broad definition of "covered stem cell lines" to ensure that human stem cells derived from any source are subject to strict ethical standards. The *Guidelines for Human Embryonic Stem Cell Research* ("National Academy of Sciences Guidelines"), a landmark document drafted by a blue ribbon committee of the National Academy of Sciences which was published May 2005, only covered embryonic stem cell lines.

These regulations create a single "gold" standard intended to ensure that all cell lines used by CIRM-funded researchers are derived according to the highest ethical standards. This revised standard has the practical implication of guaranteeing that all cell lines used by CIRM-funded researchers are derived without payment to egg donors.

These regulations require that research institutions ensure that oocyte (egg) donors do not have to pay for any immediate and short-term complications for oocyte retrieval. The National Academies' guidelines fail to address this issue.

These regulations strengthen existing regulations to make clear that it is not acceptable to provide payments for eggs (beyond reimbursement for expenses) used in CIRM-funded research under any circumstances.
These regulations go above and beyond existing state regulations and federal guidelines for assuring that potential egg donors are fully informed of their decision and the nature of the proposed research. Institutional review committees are required to approve a process for determining whether prospective donors have understood the essential aspects of the research, including but not limited to how eggs will be used and the medical risks associated with participation.

The CIRM draft regulations are substantively based on the National Academy of Sciences Guidelines. Two members of the Standards Working Group served on the NAS blue ribbon committee to develop the Guidelines. To date, the Standards Working Group has received and addressed well over thirty public comments.

Technical, Theoretical or Empirical Studies, Reports or Documents:

CIRM relied upon:

1) The National Institutes of Health Report on Stem Cells
2) The National Academy of Sciences (NAS) Guidelines for Human Embryonic Stem Cell Research, 2005, available at www.nap.edu/catalog/11278.html.
3) The National Institutes of Health Grants Policy Statement
4) Title 45, Code of Federal Regulations, Part 46 – Protection of Human Subjects
5) Public input received at five public meetings conducted by the Standards Working Group of CIRM on: July 6, 2005; August 30, 2005; October 24, 2005; December 1, 2005; and January 30-31, 2006.

Copies of the documents referenced above in numerals 1) through 4) are available on CIRM's website under the "Regulations" link at www.cirm.ca.gov. These documents are also available at the offices of CIRM located at 210 King Street, San Francisco, California, 94107. Transcripts and meeting minutes of the meetings referenced in numeral 5) are also available on CIRM's website under the "Standards Working Group" link.

Submittal of Comments:

Any interested party may present comments in writing about the proposed action to the agency contact person named in this notice. **Written comments** must be received no later than 5:00 p.m. on **May 1, 2006**. Comments regarding this proposed action may also be transmitted via e-mail to MEScomments@cirm.ca.gov or by facsimile transmission to (415) 396-9141.

A public hearing has been scheduled for the time and place stated below to receive **oral comments** regarding the proposed regulatory action.

Date: May 1, 2006

Time: 12:00 p.m. to 4:00 p.m.

Place: Elihu Harris State Building
1515 Clay Street, Training Room #11
Oakland, CA

A CIRM representative will preside at the hearing. Persons who wish to speak will be asked to register before the hearing. The registration of speakers will be conducted at the location of the hearing from 11:30a.m. to 12:00 p.m. Any other person who wishes to speak at the hearing will be afforded the opportunity to do so after the registered persons have been heard. If the number of registered persons in attendance warrants, the hearing officer may limit the time for each presentation in order to allow everyone wishing to speak the opportunity to be heard. Oral comments presented at a hearing carry no more weight than written comments.

Effect on Small Business:

CIRM has determined that the proposed regulatory action has no impact on small businesses. The regulations implement conditions on awarding grants for stem cell research. This research is conducted almost exclusively by large public and private non-profit institutions, as well as large for-profit institutions. As such, the regulations are not expected to adversely impact small business as defined in Government Code section 11342.610.

Impact on Local Agencies or School Districts:

CIRM has determined that the proposed regulatory action does not impose a mandate on local agencies or school districts, nor does it require reimbursement by the state pursuant to Part 7 (commencing with section 17500) of Division 4 of the Government Code because the regulatory action does not constitute a "new program or higher level of service of an existing program" within the meaning of section 6 of Article XIII of the California Constitution. CIRM has also determined that no nondiscretionary costs or savings to local agencies or school districts will result from the proposed regulatory action.

Costs or Savings to State Agencies:

CIRM has determined that no savings or increased costs to any agency will result from the proposed regulatory action.

Effect on Federal Funding to the State:

CIRM has determined that no costs or savings in federal funding to the state will result from the proposed regulatory actions.

Effect on Housing Costs:

CIRM has made an initial determination that the proposed actions will have no effect on housing costs.

Significant Statewide Adverse Economic Impact Directly Affecting Businesses:

CIRM has made an initial determination that adoption of this regulation will not have a significant statewide adverse economic impact directly affecting businesses, including the ability of California Businesses to compete with businesses in other states.

Cost Impacts on Representative Private Persons or Businesses:

CIRM has made an initial determination that the adoption of this regulation will not have a significant cost impact on representative private persons or businesses. The CIRM is not aware of any cost impacts that a representative private person or business would necessarily incur in reasonable compliance with the proposed action.

Impact on the Creation, Elimination, or Expansion of Jobs:

CIRM has determined it is unlikely the proposed regulatory action will impact the creation or elimination of jobs, the creation of new businesses or the elimination of existing businesses, or the expansion of businesses currently doing business within the State of California.

Consideration of Alternatives:

CIRM must determine that no reasonable alternatives considered by the agency, or that have otherwise been identified and brought to the attention of the agency, would be more effective in carrying out the purpose for which the action is proposed or would be as effective and less burdensome to affected private persons or businesses than the regulatory action.

Availability of Statement of Reasons and Text of Proposed Regulations:

CIRM has prepared an Initial Statement of Reasons, and has available the express terms of the proposed action, all of the information upon which the proposal is based, and a rulemaking file. A copy of the Initial Statement of Reasons and the proposed text of the regulation may be obtained from the agency contact person named in this notice. The information upon which CIRM relied in preparing this proposal and the rulemaking file are available for review at the address specified below.

Availability of Changed or Modified Text:

After the close of the comment period, CIRM may make the regulation permanent if it remains substantially the same as described in the Policy Statement Overview. If CIRM

does make changes to the regulation, the modified text will be made available for at least 15 days prior to adoption. Requests for the modified text should be addressed to the agency contact person named in this notice. CIRM will accept written comments on any changes for 15 days after the modified text is made available.

Agency Contact:

Written comments about the proposed regulatory action; requests for a copy of the Initial Statements of Reasons, the proposed text of the regulation, and a public hearing; and inquiries regarding the rulemaking file may be directed to:

C. Scott Tocher, Interim Counsel
California Institute For Regenerative Medicine
210 King Street
San Francisco, CA 94107
(415) 396-9100

Questions on the substance of the proposed regulatory action may be directed to:

Geoff Lomax, Senior Officer for Medical and Ethical Standards
California Institute For Regenerative Medicine
(415) 396-9134

The Notice of Proposed Regulatory Adoption, the Initial Statement of Reasons and any attachments, and the proposed text of the regulations are also available on CIRM's website, www.cirm.ca.gov.

Availability of Final Statement of Reasons:

Following its preparation, a copy of the Final Statement of Reasons mandated by Government Code section 11346.9, subdivision (a), may be obtained from the contact person named above. In addition, the Final Statement of Reasons will be posted on CIRM's webpage and accessed at www.cirm.ca.gov.

Specific Purpose and Factual Basis for each adoption:

SECTION 100010 - SCOPE

Purpose

Section 100010 establishes the scope of the regulations comprising Chapter 2. The standards contained in this chapter apply to all institutions performing research funded by the agency.

Rationale:

This section is necessary to define the circumstances and extent to which this chapter is to be applied.

SECTION 100020 - DEFINITIONS

Purpose

The following definitions shall apply to language contained in Sections 100010 through 100130 of these regulations.

(a). "Acceptably Derived." This term defines materials that may be used in CIRM-funded research. The definition refers to the materials and the manner in which they are obtained as defined further in sections 100080 and 100090. Health and Safety Code section 125290.55, subdivision (b)(2), requires CIRM to adopt standards for all medical, socioeconomic, and financial aspects of clinical trials and therapy delivery to patients, including, among others, standards for safe and ethical procedures for obtaining materials and cells for research and clinical efforts for the appropriate treatment of human subjects in medical research consistent with paragraph (2) of subdivision (b) of Section 125290.35, and to ensure compliance with patient privacy laws. This subdivision describes the materials that govern the "obtaining" of those materials.

(b). "CIRM." This acronym stands for the agency created by Proposition 71, adopted by the voters in November, 2004, the California Institute for Regenerative Medicine. This is the agency that has oversight and implementation authority for Proposition 71.

(c). "Covered Stem Cell Line." CIRM-funded research applies to a broader range of materials including but not limited to adult stem cells, fetal tissue and placenta derived cells. Proposition 71 includes definitions of "adult stem cells," "pluripotent cells," and "stem cells," (Health and Safety Code section 125292.10, subdivisions (b), (q) and (x). Also, Health and Safety Code section 125300, subdivision (a), describes the policy of the State of California involving research using many types of cells under different circumstances. This definition is consistent with the definitions already in Proposition 71 because it incorporates language consistent with the definition of the terms above. The focus on cell lines in culture alleviates concerns that scope of regulation is overly expansive.

(d). "Funded Research." This term defines "funded research" to mean research conducted with funding provided pursuant to grants issued by CIRM in accordance with Proposition 71. Because CIRM also funds grants used for training scientists in stem-cell research, the term is further defined to include these subjects, as well.

(e). "Human Subject." Certain statutes and regulations apply in the context of research conducted on or with human subjects. The definition of "human subject" is derived from the Code of Federal Regulations, Title 45, Part 46, and National Academy of Sciences

Guidelines, Number 3.1. This is a definition with which the regulated community is familiar.

(f). "Institution." This term is defined to include any public or private entity or agency, whether state, local or federal. This definition is based on the federal common rule, as embodied in the Code of Federal Regulations, Title 45, Part 46, and National Academy of Sciences Guidelines, Number 3.1. This is a definition with which the regulated community is familiar.

(g). "Institutional Review Board." Health and Safety Code section 125290.35, subdivision (b)(2), requires CIRM to adopt standards for controls on research involving humans and that these be based in part on "institutional review board"("IRB") standards. An IRB is an entity established pursuant to federal law that oversees certain federally funded research. Stem cell research conducted on humans with federal funds must be approved by an IRB. This term is defined to mean those boards created pursuant to federal regulation.

(h). "Permissible Expenses." Health and Safety Code section 125290.35, subdivision (b)(3), prohibits compensation to research donors or participants but allows reimbursement of expenses. "Permissible expenses" means necessary and reasonable costs directly incurred as a result of donation or participation in research activities. Permissible expenses may include but are not limited to costs associated with travel, housing, child care, medical care, health insurance and actual lost wages.

(i). "Research." These regulations apply to training grants as well as research funded by CIRM. This term based on and consistent with the federal definition, as contained in the Code of Federal Regulations, Title 45, Part 46, and National Academy of SciencesGuidelines, Number 3.1. This definition is therefore one with which the regulated community has experience and is familiar.

(j.) "Somatic Cell Nuclear Transfer (SCNT)." This term means the transfer of a cell nucleus from a somatic cell into an oocyte from which the nucleus has been removed. This definition is based on that of the National Institutes of Health definition at the federal level and is consistent therewith.

(k). "Stem Cell Research Oversight Committee." This terms means a committee established in accordance with 17 California Code of Regulations, Section 100060. The purpose is to provide oversight of all issues related to derivation and use of human embryonic stem ("hES") cell lines and to facilitate education of investigators involved in hES cell research.

Rationale:

To make specific the language and terminology used in formulating regulations.

SECTION 100030 – ACTIVITIES NOT ELIGIBLE FOR CIRM FUNDING:

Purpose:

This section defines research activities not eligible for CIRM funding. They include human reproductive cloning, the in vitro culture of 1) any intact human embryo or 2) any product of SCNT after appearance of the primitive streak or after 12 days, whichever is earlier. The 12-day period does not include time the embryo and/or cells have been stored frozen. Also prohibited are the introduction of stem cells from a covered stem cell line into nonhuman primate embryos, the introduction of stem cells into human embryos, and the breeding of any animal into which stem cells from a covered stem cell line have been introduced. The purpose of these restrictions is to ensure compliance with existing state and federal policy in this area.

Rationale: California Health and Safety Code Sections 125292.10, subdivision (b), and 125290.35, subdivision (b)(6), prohibit human reproductive cloning and a limit on time during which cells may be extracted from blastocysts beyond 8 to 12 days, respectively. The CIRM is charged with adopting standards applicable to the use of cells in research funded by the agency. The remaining provisions of the regulation are direct recommendations of the National Academy of Sciences Guidelines and are considered necessary elements to ensure ethical and appropriate conduct of stem cell research.

SECTION 100040 – INSTITUTIONAL ASSURANCE OF COMPLIANCE:

Purpose:

CIRM is responsible for ensuring grantees comply with the Act and applicable regulations. All research institutions shall be responsible for providing written assurance satisfactory to CIRM that CIRM-funded research complies with the requirements set forth in this chapter. To further ensure that compliance, the regulation specifies that each institution shall 1) designate an institutional official responsible for oversight of and documentation of compliance for CIRM-funded research; 2) designate one or more SCRO committee(s) established in accordance with the requirements of Title 17, California Code of Regulations, Section 100060; 3) designate one or more Institutional Review Boards; and 4) ensure that clinical personnel who have a conscientious objection not be required to participate in providing donor information or securing donor consent for research use of gametes or embryos.

Rationale:

This regulation is necessary to ensure CIRM is able to monitor compliance among recipients with critical state laws and regulations. Health and Safety Code section 125300, subdivision (b), states that research involving the derivation and use of human embryonic stem cells, germ cells, and adult stem cells, in addition to others, shall be reviewed by an approved institutional review board. The remaining provisions embody National Academy Guidelines adopted to guide federally funded research in this area.

The establishment of an SCRO ensures that proposed research is reviewed by an expert panel to ensure the research is permissible and ethical. The SCRO is the best method to ensure proper oversight of all issues related to derivation and use of human embryonic stem cells. These provisions ensure consistency where possible with important federal guidelines and embody common practice in this area.

SECTION 100050 – COMPLIANCE:

Purpose:

This section states that grantees must report promptly to CIRM any failure to comply with the terms and conditions of an award. Depending on the severity and duration of the non-compliance, consequences for failure to comply with the terms and conditions are identified.

Rationale:

This regulation is necessary to ensure that CIRM grantees are under obligation to inform CIRM when there has been a failure of compliance. In light of the fact that research is not conducted by CIRM staff nor is CIRM staff available at the site of research to provide uniform monitoring of all grantee activities, self-reporting is the most cost-effective method to ensure CIRM is aware of difficulties in complying with the law. These provisions are based on the National Institutes of Health Grants Policy Statement (Dec. 2003) and thus provides consistency with institutions familiar with federal policy and practice in this area.

SECTION 100060 – SCRO MEMBERSHIP AND FUNCTION:

Purpose:

The purpose of this regulation is to describe the composition and functions of the designated SCRO committee. The purpose of the SCRO is to provide scientific and ethical review of CIRM-funded research consistent with the requirements of Section 100070 and other applicable CIRM requirements.

Rationale:

This regulation is necessary to provide grantees guidance on the composition and function of the SCRO in overseeing stem cell research funded by the CIRM. The SCRO is a requirement embodied in section 100040. The membership, function and SCRO investigator functions are derived directly from recommendations contained in the National Academy of Sciences Guidelines. The regulation provides flexibility that allows multiple institutions to use the same SCRO to address resource or expertise realities. It is necessary to define the membership and functions to ensure efficient and consistent administration of grantee research.

100070 – SCRO REVIEW AND NOTIFICATION:

Purpose:

(a) This section states that CIRM-funded research involving derivation of covered stem cell lines or use of human oocytes or embryos in stem cell research may not commence without SCRO committee review and approval in writing. The designated SCRO committee may require that modification be made to proposed research or documentation of compliance with the requirements of subdivision (a)(3) of this regulation as a condition of granting its approval. This regulation identifies the criteria the investigator must address in the research proposal.

(b) CIRM-funded research introducing covered stem cell lines into human or non-human animals at any state of embryonic, fetal, or postnatal development may not commence without SCRO committee review and approval in writing. This section identifies the elements the SCRO must consider in evaluating when to approve such research.

(c) CIRM-funded purely in vitro research utilizing covered stem cell lines may not commence without written notification to the designated SCRO Committee. This section identifies the minimum contents of the notice.

Rationale:

(a) This section is necessary to ensure consistency in administration of research involving stem cells. The requirements for SCRO approval for CIRM-funded derivation, the demonstration of expertise, documentation of compliance with necessary review, and documentation of how cell lines will be characterized are based on recommendations of the National Academy of Sciences. This section is necessary to ensure a consistent oversight process that will help ensure that research with human embryonic stem cells is conducted in a responsible and ethically sensitive manner.

(b) This section is necessary to ensure that these requirements pertain to all cell lines used by CIRM-funded researchers. The requirements to evaluate probably pattern of differentiation and document compliance with necessary review ensures consistent oversight process that will help ensure that research with human embryonic stem cells is conducted in a responsible and ethically sensitive manner. Likewise, these requirements are based on recommendations adopted by the National Academy of Sciences.

(c) This section is necessary to assure consistent oversight process that will help ensure that research with human embryonic stem cells is conducted in a responsible and ethically sensitive manner. This requirement is consistent with CIRM's grants administration policy and National Academy of Sciences Guidelines. The intent is to ensure that all CIRM-funded research is adequately tracked at the institution. The type of research covered in this section does not necessitate formal "scientific and ethical review" because it does not involve human subjects. None the less, it is critical for

purposes of complete oversight that the SCRO be aware of research being performed at the institution. This provision requires a notification mechanism.

SECTION 100080 – ACCEPTABLE RESEARCH MATERIALS:

Purpose:

The purpose of this section is to require that all covered stem cell lines used in CIRM-funded research be acceptably derived. Each subdivision identifies particular criteria that meet the definition of "acceptably derived." Subdivisions (a) through (c) permit use of stem cells approved by the National Institutes of Health, deposited in the United Kingdom Stem Cell Bank or used or approved by a licensee of the United Kingdom Human Fertilization and Embryology Authority. Subdivision (d) permits use of cells derived in accordance with the Canadian Institutes of Health under applicable regimes.

(e) This section identifies 5 conditions on the use of cells; 1) requiring informed consent of donors; 2) assurance the donors have not been compensated for their donation; 3) prohibiting purchase or sale of gametes, embryos, somatic cells or human tissue, except as provided in subdivision (e)(2) of this regulation (permitting reimbursement for permissible expenses); 4) that donation of materials was overseen by an IRB or IRB equivalent; that donors who consented to donate stored materials were not reimbursed for the cost of storage prior to the decision to donate.

Rational:

This section is necessary to fulfill the requirement that CIRM establish the appropriate regulatory standards and oversight bodies for research and facilities development, pursuant to the State Constitution. Health and Safety Code section 125290.35, subdivision (b), requires CIRM establish standards for obtaining informed consent of research donors and participants, standards prohibiting compensation to research donors (but allow reimbursement for expenses), and limits payments for the purchase of stem cells or stem cell lines (except for reasonable payments for expenses associated with the handling of such materials).

The entities identified in subdivisions (a) through (d) meet standards established by the National Institutes of Health or otherwise meet standards identified by the Standards Working Group. As such, these subdivisions are necessary to address the issue of stem cells lines created prior to enactment of Proposition 71 and define the permissible lines for use in CIRM-funded research. This allows needed flexibility and ensures availability of acceptable stem cell lines for CIRM-funded research ensuring proper standards are adhered to.

Subdivision (e)(1) is necessary to ensure compliance with Health and Safety Code requirement that donors have provided informed and voluntary consent. This also is considered a fundamental protection under federal law (see Code of Federal Regulations, Title 45, Part 46) and National Academy of Sciences Guidelines, number 3.1.

Subdivision (e)(2), prohibiting donors from receiving valuable consideration, is required by Health and Safety Code section 125290.35, subdivision (b)(3), as a standard prohibiting compensation. This term, as defined above in Section 100020, subdivision (h), provides clarity by defining permissible expenses that may be reimbursed.

Subdivision (e)(3) is necessary to ensure that all persons, in addition to donors, to not receive valuable consideration for the purchase or sale of stem cells or other similar materials. This section implements Health and Safety Code section 125290.35, subdivision (b)(5), which does allow payments for removal, storage, processing, and other handling of stem cells.

Subdivision (e)(4) is necessary to ensure that material donation is overseen by an IRB or its equivalent. This is consistent with federal law, which makes the IRB responsible for ensuring fundamental protection under federal law and is a major recommendation of the National Academy Guidelines for stem cell research. Moreover, this provision is consistent with California Health and Safety Code section 125300, which requires IRB oversight of various aspects of donation of gametes, embryos and tissue.

Subdivision (e)(5), prohibiting compensation for storage costs for those who elect to donate stored blastocysts, is necessary to ensure compliance with the statutory prohibition of compensation and ensures that payment of such costs is not an inducement to donate. This provision is consistent with National Academy Guidelines, Number 3.4, subdivision (a), governing stem cell research.

SECTION 100090: ADDITIONAL REQUIREMENTS FOR CIRM-FUNDED RESEARCH:

Purpose:

This section identifies further requirements with which the SCRO must affirm compliance when CIRM funds are used to derive new human stem cell lines. These requirements are in addition to those required by Section 100080, subdivision (e).

(a) The SCRO must confirm that donors of material have given voluntary and informed consent (as set forth in Section 100900).

(b) Where obtaining oocytes is required for derivation, the SCRO must confirm that the following conditions have been met – that the donor's fertility treatment has not been compromised; the funded institution has agreed to assume the cost of medical care required as a result of the donation for research; that the physician attending the donor and the principal investigator are not the same person (unless approved by the IRB); and that the physician performing oocyte retrieval not have a financial interest in the outcome of the research.

Rationale:

(a) Health and Safety Code Section 125290.35, subdivision (b)(1), requires CIRM establish standards for obtaining the informed consent of research donors, patients or participants. This section is necessary to ensure that documentation by the proper oversight authority has ensured that the requirements of Section 100100 have been met.

(b) These requirements are based on public input and National Academy Guidelines to establish protections for prospective donors necessary to ensure donors are not exploited. Ensuring the attending physician and principal investigator are not the same individual is designed to erect a barrier against competing interests in oocyte donation. This ensures that oocyte donation will not come at the expense of the best interests of the patient, medically, and is consistent with National Academy Guidelines (3.5). Ensuring the physician does not have a financial interest in the research outcome will help to minimize potential undue influence in oocyte donation circumstances.

SECTION 100100 – INFORMED CONSENT REQUIREMENTS:

Purpose:

(a). Subdivision (a) states that all CIRM-funded research on human subjects is subject to Federal and state law governing human subject research and informed consent. Existing law provides that state requirements contained in California Health and Safety Code Section 24173 regarding informed consent do not apply to certain research within an institution that holds federal assurance and that has obtained informed consent in the method and manner required under federal law.

(b). This subdivision prohibits conduct of human subject research that violates documented donor preferences with regard to use of donated materials. To ensure fully informed disclosure the subparts of this subdivision identifies the information that must be disclosed to donors.

(c). ResearcheRs must provide donors with the opportunity to describe permissible uses for donated materials. The regulation also permits researchers to use only materials from donors who have agreed to all future used for donated materials.

(d). This subdivision identifies additional disclosure requirements that must be made by researchers to donors that apply in the context of human egg donation. These requirements are intended to ensure documented informed consent.

(e). For CIRM-funded research involving the donation of embryos for stem cell research, the informed consent process shall include a statement that embryos will be destroyed in the process of deriving embryonic stem cells.

(f). For CIRM-funded research involving the donation of the umbilical cord, cord blood or the placenta, consent shall be obtained from each known legal parent, guardian or

progenitor. Informed consent shall include a statement as to whether the donated cells may be available for autologous treatment in the future.

(g). For CIRM-funded research involving the donation of somatic cells for SCNT, informed consent shall include a statement as to whether the donated calls may be available for autologous treatment in the future.

Rationale:

California Health and Safety Code Section 125290.35, subdivision (b)(1), requires CIRM to adopt standards for informed consent of donors. The following provisions are considered necessary to implement the requirement of this statute in a manner reflecting the best practices of existing research and draws on federal guidelines with which institutions are familiar.

(a). This subdivision is necessary to describe the parameters of existing law and identify the circumstances under which this regulation does not apply. California Health and Safety Code Section 24178, subdivision (a), states that Section 24173 shall not apply to any person who is conducting a medical experiment as an investigator within an institution that holds an assurance with the United States Department of Health and Human Services pursuant to Part 46 of Title 45 of the Code of Federal regulations and who obtains informed consent in the method and manner required by those regulations.

(b). This subdivision applies several rules. The rule providing that research not violate the preferences of donors is necessary to ensure the integrity of the donor system that is integral to obtaining materials essential to stem cell research. This rule embodies National Academy Guidelines (3.6) that provide that donors could be offered the option of agreeing to some forms of human embryonic cell research but not others and that the consent process should fully explore whether donors have objections to any specific forms of research to ensure that their wishes are honored.

The informed consent requirements are consistent with existing the National Academy Guidelines and existing California regulations. A statement that cells may be kept for many years is already part of California Health and Safety Code section 125315, as well as part of NAG 3.6(f).

The National Academy Guidelines (3.6(d)) recommend that if the identities of donors are retained, the donor be informed as to whether he or she wishes to be contacted in the future to receive information obtained trough studies of the stem cell lines. This recommendation is embodied subdivision (b)(2).

Through feedback and work of the Standards Working Group, it was determined that it was necessary to emphasize to donors that future uses may exist for research that may be unknown at the time of the donation (subdivision (b)(3)). This is necessary to ensure that donors are informed that research topics and subject areas are evolving and that their material may, with their consent, be used for such studies if the donor chooses.

Subdivision (b)(5) requires a statement that cells may be transplanted into humans or animals. This statement is necessary in light of existing research practices, is considered a subject that might be relevant to some donors and for which consent should be obtained or awareness established. This is consistent with National Academy Guidelines recommendations (3.6(g)).

Subdivision (b)(6) clarifies that no direct medical obtains to the donor by virtue of the donation, except in obvious cases where the donation is autologous in nature, for the benefit of the donor. This clarification seeks to avoid potential confusion surrounding donation and is consistent with concerns identified by the National Academy Guidelines (3.6)(i)).

Subdivision (b)(7) clarifies that donations are made without restriction on who may be the recipient of the transplants of the cells derived, except in the obvious case where the donor is the intended recipient. This clarification ensures avoidance of potential confusion surrounding donation and is consistent with concerns identified by the National Academy Guidelines (3.6(b)).

Subdivision (b)(8) seeks to assure that patients do not feel coerced into donation materials and assures that neither consenting to nor refusing to participate in donation will have any effect on quality of any future care provided to the potential donor. This clarification ensures avoidance of potential confusion surrounding donation and is consistent with concerns identified by the National Academy Guidelines (3.6(k)).

Subdivision (b)(9) is necessary to make the potential donor aware of the fact that study involving the donor's materials may have a commercial potential but that the donor will not received financial or any other benefits from any future commercial development. This clarification ensures avoidance of potential confusion surrounding donation and is consistent with concerns identified by the National Academy Guidelines (3.6(h)). This already is a required element comprising informed consent in the context of materials used obtained during fertility treatment (California Health and Safety Code Section 125315, subdivision (c)(5)).

(c). Subdivision (c) embodies National Academy Guidelines recommendations (3.6(h)) that the consent process should fully explore whether donors have objections to any specific forms of research to ensure that their wishes are honored. The Standards Working Group has determined that this element in the regulation is necessary to ensure that such objections have the opportunity for expression.

(d). Subdivision (d) – The Standards Working Group has identified oocyte donation issues as particularly complex and controversial and thus requiring specials standards. Particular risks associated with egg donation have been identified and comprise the substantive disclosure requirement in (d)(1) of the regulation. This is consistent with federal regulation on point in the context of federal funding (Title 45 CFR, Part 46).

Existing law (Health and Safety Code Section 24173, subdivision (c)(11)) requires that any material financial stake or interest that the investigator or research institution has in the outcome of the medical experiment be disclosed. Accordingly, this requirements is embodied in the context of oocyte donation under subdivision (d)(2) of this regulation to ensure potential donors are aware of any potential for conflicts of interest on behalf of researchers.

Subdivision (d)(3) provides for necessary time to ensure that the donor fully understands what the donor is consenting to and is provided time upon which to reflect on the information given and to weigh the factors present in the decision. Similarly, subdivision (d)(4) is necessary to ensure that there is actual comprehension of the factors involved in the donation and that the consent being given or withheld is truly informed. This subdivision provides flexibility for researchers to determine that the donor understands fundamental and essential aspects of the research.

(e). This subdivision requires clarification with the donor that there is an understanding that embryos will be destroyed in the process of deriving human embryonic stem cells. This clarification ensures avoidance of potential confusion surrounding donation and is consistent with concerns identified by the National Academy Guidelines (3.6(j)).

(f). This subdivision is seen as a necessary extension of National Academy Guidelines to address cord blood and placenta. This clarification is necessary to ensure avoidance of potential confusion surrounding donation of these materials and identifies from whom the consent shall be derived. This is necessary to ensure consistent application of the law and ensure the proper consent is derived from necessary individuals.

(g). This subdivision is necessary to ensure that donors are aware as to whether donated cells for SCNT may be available for autologous treatment in the future. This clarification ensures avoidance of potential confusion surrounding donation and is consistent with concerns identified by the National Academy Guidelines (3.6(i)).

SECTION 100110 - FAIRNESS AND DIVERSITY IN RESEARCH:

Purpose:

The purpose of this section is to require compliance with the California Health Research Fairness Act, and Inclusion of Women and Minorities in Clinical Research Act.

Rationale:

The California Health Research Fairness Act, California Health and Safety Code, Sections 439.900-439.906, and Inclusion of Women and Minorities in Clinical Research Act, Health and Safety Code, Sections 100237-100239, state California policy with respect to research fairness and the inclusion of women and minorities in clinical research funded by the State of California. The Standards Working Group identified fairness and

inclusion as a priority and composed this section to ensure that existing state policies and law regarding research clearly applies in the context of CIRM-funded research.

SECTION 100120 – RECORD KEEPING:

Purpose:

This section requires grantee institutions to maintain described records that concern CIRM-funded research activities. The subdivisions of this section require a research registry contain necessary documentation of CIRM-funded stem cell research conducted by the institution; pertinent review or notification requirements as required in Section 120600 of these regulations; the methods utilized to characterize and screen the materials for safety; the conditions under which the materials have been maintained and stored, where applicable; record of all gametes, somatic cells, embryos or products of SCNT that have been donated, created or used so as to determine the provenance and disposition of such materials. The section also requires a cross-reference for additional documentation that may be required by CIRM.

Rationale:

This regulation is necessary to ensure compliance with requirements imposed on the CIRM to track the use of CIRM funds and to ensure compliance with applicable statutes and regulations. National Academy Guidelines (6.1) state that institutions should required documentation of the provenance of all human embryonic stem cell lines, whether the cells were imported into the institution or generated locally. Notice to the institution should include evidence of IRB-approval of the procurement process, evidence of and adherence to basic ethical and legal principles of procurement, as indicated in the recommendation. In the case of lines imported from another institution, it is recommended that documentation that these criteria were met at the time of derivation will suffice. This section ensures the integrity of the donation process is assured and that future use of particular stem cell lines and materials can comply with necessary provenance and derivation requirements.

SECTION 100130 – MATERIALS SHARING:

Purpose:

The purpose of this section is to require that stem cell lines and biomedical materials developed with CIRM funding at academic, commercial research and development organizations be broadly disseminated. CIRM-funded research institutions must comply with any CIRM-Intellectual Property regulations intended to ensure data and materials sharing.

Rationale:

This regulation is necessary to cross reference CIRM regulations pertaining to inventions and other intellectual property that may pertain to grantees. This regulation adds nothing substantive beyond that which may be required from time to time by CIRM Intellectual Property regulations but ensures that grantees are aware that such particular requirements may be applicable.